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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/207,649    12/08/98    LINDQUIST    S    ARCD:278

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EXAMINER

TURNER, S

ART UNIT

PAPER NUMBER

1647

14

DATE MAILED: 10/24/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.

09/207,649

Applicant(s)

Lindquist

Examiner

Sharon L. Turner, Ph.D.

Group Art Unit

1647



☒ Responsive to communication(s) filed on 8-1-00

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claim

☒ Claim(s) 1, 3, 4, 7-20, 22, and 37-40 is/are pending in the application.

Of the above, claim(s) 38-40 is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1, 3, 4, 7-20, 22, and 37 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☒ Claims 1, 3, 4, 7-20, 22, and 37-40 are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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## **DETAILED ACTION**

### ***Continued Prosecution Application***

1. The request filed on 8-1-00 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09207649 is acceptable and a CPA has been established. An action on the CPA follows.

### **Response to Amendment**

2. The Art Unit of U.S. Patent application SN 09/<sup>207,649</sup>~~030,157~~ has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Examiner Turner, Technology Center 1600, Art Unit 1647.
3. The amendment filed 8-01-00 has been entered into the record and has been fully considered. Claims 23-36 are canceled. Claims 1, 3, 4, 7-20, 22 and 37-40 are pending.
4. Newly submitted claims 38-40 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: New claims 37-39 are drawn to methods of identifying candidate substances that inhibit the formation of amyloid fibrils. This is in contrast to methods of identifying candidate substances that inhibit the formation of amyloid aggregates. Fibrils are distinct structures from aggregates because fibrils are ordered structures of beta amyloid found in Alzheimer's brains and exhibit rod-like and beta-sheet conformations. In contrast, aggregates merely constitute clustered, closely associated or bound proteins.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution

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on the merits. Accordingly, claims 38-40 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

5. As a result of applicants amendment, all rejections not reiterated herein have been withdrawn by the examiner.

### ***Claim Objections***

6. Claim 4 and dependent claims thereof 7-14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The recitation "wherein the mammalian aggregate-prone amyloid protein is a chimeric protein" broadens the scope of the claim to encompass amino acids which are not recognized as amyloid peptides and thus do not further limit but broaden the independent claim.

### ***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 4 and 7-14 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mammalian prion proteins and mammalian amyloid peptides, does not reasonably provide enablement for a mammalian aggregate-prone amyloid protein wherein the protein is a chimeric protein. The specification does not enable any person

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skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. Claims 4 and 7-14 recite mammalian peptides which are chimeric. The skilled artisan as taught by Lazar et al, Molecular and Cellular Biology, 8(3):1247-52, March 1988 recognizes that proteins are highly dependent upon sequence structure and that a single mutation of a protein can affect the biological activities of the molecule. Thus, from the purposes of this discussion a mammalian polypeptide which has not been shown to be naturally occurring and contains mutations in specific residues, can not be considered the same protein. The mutated protein then contains a foreign sequence and may be considered a chimera. Applicants amendment to the recitation of mammalian proteins appears to limit the invention to naturally occurring proteins. However, fusion proteins contain foreign DNA, such as recited in claims 4 and 7-14, in particular the claim recites proteins operably attached to a detectable marker, are proteins which are considered to contain foreign DNA and thus constitute chimeras. The specification defines no mammalian chimeras. In view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention..

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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10. Claims 4 and 7-14 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 4-14 are indefinite as the skilled artisan is not reasonably apprised of the metes and bounds of a mammalian chimeric protein. It is contradictory that a mammalian protein is a chimeric protein (a protein having foreign sequences). In addition, the recitation "an aggregate forming domain" is indefinite because the skilled artisan has no guidance by which to determine that portion of a chimeric protein which forms "an aggregate forming domain."

11. Claims 3, and 12-14 stand rejected under 35 U.S.C. 112, second paragraph, as set forth in Paper No. 5, mailed 8-4-99 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant argues that one of skill in the art would recognize what is meant by "PrP or  $\beta$ -amyloid polypeptide," that the claims are not directed to prion proteins and that the claims also recite a mammalian aggregate-prone amyloid protein...under conditions effective to allow aggregated amyloid formation," which provides the skilled artisan with additional information as to the scope of the claims.

These arguments have been fully considered but are not persuasive. The skilled artisan recognizes a multitude of forms of prion proteins and the specification contains reference to a PrP<sup>c</sup> and PrP<sup>sc</sup>. The specification refers to PrP (the mammalian prion protein), see in particular p. 5, line 2. However, the specification does not further define a PrP and the metes and bounds

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of a PrP is unclear to the skilled artisan even though a PrP appears to refer to one of many recognized forms of mammalian prion proteins. A name by itself does not structurally define a protein without specific references. Wickner is relevant as it teaches that the skilled artisan recognizes that prion proteins have divergent structures and share the characteristics as specified. Thus applicants have not clarified the metes and bounds of a mammalian PrP. In addition, the skilled artisan recognizes a multitude of amyloid proteins which are capable of aggregate formation. The skilled artisan also recognizes that many proteins aggregate (a relative term). However, the skilled artisan does not specifically recognize a "mammalian aggregate-prone amyloid protein." Applicants contemplate aggregate-prone amyloid proteins, to be of essentially any origin, and having the ability to aggregate under physiological conditions such as inside of a cell, page 5, lines 16-23. As the metes and bounds of "aggregate" are unclear and applicants contemplation of amyloid proteins appears to contradict the structural limitations recognized in the art, the metes and bounds of the claims remain unclear.

***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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13. Claims 1, 3-4, 7, 12-13, and 17-18 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hughes et al, PNAS, 93:2065-70, 1996 as set forth in Paper No. 5, mailed 8-4-99. Claims 8-11, 14-16, 19, 20 and 22 are rejected as depending from a rejected base claim.

Applicant argues that the assay employed in the Hughes et al reference measures an interaction between two monomers, that the two-hybrid system is set up to evaluate only interactions between single polypeptides, that the system is not compatible with the formation of aggregates.

Contrary to applicants assertion, the Hughes reference clearly measures the interaction of A $\beta$  peptide aggregates as evidenced in Figure 1. Applicants have not defined their invention to exclude the interaction of A $\beta$  monomers. The A $\beta$  monomers of Hughes clearly interact as evidenced by the expression of the reporter gene lacZ and that direct interaction constitutes an aggregation as depicted in Figure 1. The A $\beta$  TT mutant is an identified substance which inhibits aggregation. Thus, Hughes anticipates the claimed invention.

14. Claims 4 and 7-14 stand rejected under 35 U.S.C. 102(b) as set forth in Paper No. 5, mailed 8-4-99 as being anticipated by IDS Ref., Wickner et al, Chernoff et al, Paushkin et al, and Patino et al.

Applicants argue that the references do not anticipate the claims as amended to recite mammalian aggregate-prone amyloid proteins.

These arguments are not persuasive as claims 4-14 recite mammalian aggregate-prone amyloid proteins wherein the proteins are chimeric and in particular the claimed embodiments

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include chimeric proteins comprising Sup35 (a yeast protein) in which the N-terminal domain has been replaced by amino acids 1-42 of  $\beta$ -amyloid protein. Since amyloid and prion proteins share sequences in common and since such sequences may influence aggregation the references teachings with respect to yeast proteins appears to be no different than those proteins claimed as chimeras. Thus, the reference teachings anticipate the claimed invention.

15. Claims 1, 3, 15, 17-19 and 37 stand rejected under 35 U.S.C. 102(b) as being anticipated by Cordell et al, WO91/04339, 4 April, 1991. Claims 4, 7-14, 16, 20, 22 and 37 are rejected as depending from a rejected base claim.

Cordell et al teach assays and reagents for amyloid deposition including the identification of agents which inhibit amyloid formation. The amyloid products produced may be expressed in yeast and include beta-amyloid 1-42 and preamyloid precursors, in particular p. 6, lines 5-30 and p. 7, line 13 and p. 11, lines 3-28. The amyloid aggregates are detected by Congo red, thioflavin S or silver salt staining which are indicative of fibrillary material, in particular p. 13, lines 20-36. Aggregates may be detected by attachment of antibodies or other labels such as fluorescent enzymatic or radioactive labels, in particular, pps. 14-15, especially p. 15, lines 5-6. Thus, the reference teachings anticipate the claimed invention.

#### **Status of Claims**

16. No claims are allowed.

#### **Conclusion**

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17. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.  
October 22, 2000

**CHRISTINE SAOUD**  
**PATENT EXAMINER**

*Christine Saoud*